

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

What is claimed is:

1. (Currently amended) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

- (a) providing a first assay system capable of detecting mitogen-activated protein kinase kinase 6 (MAP2K6) expression or activity comprising a MAP2K6 polypeptide or nucleic acid;
- (b) contacting the assay system of step (a) with a candidate test agent;
- (c) measuring the expression or activity of MAP2K6 in the presence or absence of the test agent;
- (d) identifying a candidate branching morphogenesis modulating agent by detecting a change in the expression or activity of MAP2K6 in the presence of the test agent compared with no test agent;
- (e) providing a second assay system capable of detecting a change in the branching morphogenesis pathway comprising cultured cells or a non-human animal expressing MAP2K6;
- (f) contacting the assay system of step (e) with the candidate test agent of (b);
- (g) measuring the branching morphogenesis pathway in the presence or absence of the test agent; and
- ~~(g)~~ (h) confirming that the test agent of (b) is a candidate branching morphogenesis modulating agent by detecting a change in the branching morphogenesis pathway in the presence or absence of the test agent.

2. (Previously presented) The method of Claim 1, wherein the first assay system includes a screening assay comprising a MAP2K6 polypeptide, and the candidate test agent is a small molecule modulator having a molecular weight less than 10,000 daltons.

3. (Previously presented) The method of Claim 2, wherein the screening assay is a kinase assay.

4. (Currently amended) The method of Claim 1, wherein the first assay system includes a binding assay comprising ~~an~~ a MAP2K6 polypeptide and the candidate test agent is an antibody.

5. (Currently amended) The method of Claim 1, wherein the first assay system includes an expression assay comprising ~~an~~ a MAP2K6 nucleic acid and the candidate test agent is a nucleic acid modulator molecule.

6. (Previously presented) The method of Claim 5, wherein the nucleic acid modulator molecule is an antisense oligomer.

7. (Previously presented) The method of Claim 6, wherein the nucleic acid modulator molecule is a phosphorothioate morpholino oligomer (PMO).

8.– 14. (Canceled)

15. (Currently amended) The method of Claim 34, wherein the assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic mouse tumor assay.

16. (Currently amended) The method of Claim 15, wherein the assay system includes a transgenic mouse tumor assay that includes a mouse comprising a RIP 1-Tag2 transgene.

17. (Canceled)

18. (Previously presented) The method of Claim 1, wherein the second assay system includes an assay that detects a change in an activity associated with angiogenesis.

19. (Previously presented) The method of Claim 1, wherein the second assay system comprises cultured cells.

20. (Previously presented) The method of Claim 19, wherein the second assay system includes an assay that detects an event selected from the group consisting of cell proliferation, cell cycling, apoptosis, tubulogenesis, cell migration, cell sprouting and response to hypoxic conditions.

21. (Previously presented) The method of Claim 20, wherein the second assay detects tubulogenesis or cell migration or cell sprouting, and wherein the second assay system comprises the step of testing the cellular response to stimulation with at least two different pro-angiogenic agents.

22. (Previously presented) The method of Claim 20, wherein the assay detects tubulogenesis or cell migration, and wherein cells are stimulated with an inflammatory angiogenic agent.

23. (Canceled)

24. (Currently amended) The method of Claim 35, wherein the assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic mouse tumor assay.

25. (Currently amended) The method of Claim 24, wherein the assay system includes a transgenic mouse tumor assay that includes a mouse comprising a RIP1-Tag2 transgene.

26. (Original) A method of modulating branching morphogenesis in a mammalian cell comprising contacting the cell with an agent that specifically binds a MAP2K6 polypeptide or nucleic acid.

27. (Previously presented) The method of Claim 26, wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with branching morphogenesis.

28. (Previously presented) The method of Claim 26, wherein the agent is a small molecule modulator having a molecular weight less than 10,000 daltons, a nucleic acid modulator molecule, or an antibody.

29. (Previously presented) The method of Claim 26, wherein the branching morphogenesis is angiogenesis.

30. (Previously presented) The method of Claim 29, wherein tumor cell proliferation is inhibited.

31. (Previously presented) A method for diagnosing prostate, stomach, or testis cancer in a patient comprising:

- (a) obtaining a biological sample from the prostate, stomach, or testis of a cancer patient;
- (b) contacting the biological sample with a probe for MAP2K6 expression;
- (c) comparing results from step (b) with a tissue-matched control biological sample;
- (d) detecting an elevated level of MAP2K6 expression in the biological sample of step (a) compared with the tissue-matched control biological sample; and
- (e) determining whether step (d) indicates a likelihood of prostate, stomach, or testis cancer.

32. (Canceled)

33. (Canceled)

34. (Previously presented) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

- (a) providing an assay system comprising a nonhuman animal expressing MAP2K6, wherein the assay system includes an assay that detects an agent-biased change in branching morphogenesis;

- (b) contacting the assay system of step (a) with a candidate test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and
- (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent.

35. (Previously presented) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

- (a) providing an assay system comprising a MAP2K6 polypeptide or nucleic acid;
- (b) contacting the assay system of step (a) with a candidate test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity;
- (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent;
- (d) providing a second assay system comprising a non-human animal expressing MAP2K6, wherein the second assay system includes a second assay that detects an agent-biased change in an activity associated with branching morphogenesis;
- (e) contacting the second assay system with the candidate test agent of (b) under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and
- (f) detecting an agent-biased activity of the second assay system, wherein a difference between the agent-biased activity and the reference activity of the second assay system confirms the candidate test agent as a candidate branching morphogenesis modulating agent.